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| 10/594,432 | 11/16/2007 | Zhongxin Ge | 1034136-000035 | 2929 |

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| EXAMINER |
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MCCRACKEN, DANIEL

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| ART UNIT | PAPER NUMBER |
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1793

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| NOTIFICATION DATE | DELIVERY MODE |
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06/21/2010

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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| Office Action Summary | Application No. 10/594,432 | Applicant(s) GE ET AL. | |
| | Examiner DANIEL C. MCCracken | Art Unit 1793 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 September 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1 and 5-20 is/are rejected.
- 7) ☒ Claim(s) 2-4 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 26 September 2006 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Citation to the Specification will be in the following format: (S. # : ¶/L) where # denotes the page number and ¶/L denotes the paragraph number or line number. Citation to patent literature will be in the form (Inventor # : LL) where # is the column number and LL is the line number. Citation to the pre-grant publication literature will be in the following format (Inventor # : ¶) where # denotes the page number and ¶ denotes the paragraph number.

Status of Application

This office action is in reply to the papers as filed 9/26/2006. Claims 1-20 are pending.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 9/26/2006 and 4/9/2007 are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements are being considered by the examiner.

Drawings

The drawings are objected to as failing to comply with 37 CFR 1.84(p)(5) because they include the following reference character(s) not mentioned in the description: Reference numerals 1-6 in Figures 1-2. Corrected drawing sheets in compliance with 37 CFR 1.121(d), or amendment to the specification to add the reference character(s) in the description in compliance with 37 CFR 1.121(b) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing

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on the immediate prior version of the sheet, even if only one figure is being amended. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

I. Claims 7-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

With respect to Claim 7, the "R" and "Q" groups are not defined by the claim. This, coupled with the permutations and combinations of subscripts, make determining the scope of the claim impossible. While "R" may be conventionally used to denote an alkane, dependent claims suggest that R can represent much more than conventional alkanes – *see e.g.* Claims 8, 10. Furthermore, "Q" - insofar as the Examiner is aware - is not conventionally used to denote anything, nor is there an explicit definition in the specification. The description of the compound at (S. 7: 24-25) is confusing in that it is unclear whether the Q group is derivatizing the R group (which is how the passage reads) or the PEG monomer as suggested by the chemical formula. Thus, it is not clear what is encompassed by the claim: Can R (which can apparently cover anything and everything) be functionalized by Q (which can cover anything and everything), or

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is Q to be bonded to the PEG moiety? Claims 8-16 import the indefiniteness issues associated with Claim 7.

With respect to Claim 17, it is not entirely clear what structure is required by each step. The claim recites “reacting a malonyl-polyethylene glycol” but yields a “pegylated trimetallic nitride endohedral metallofullerene.” It is unclear whether the malonyl group is required by the claim or not. This is especially relevant for Claim 20, a product-by-process claim. Process limitations are not given weight except to the extent they suggest structural or compositional features. *See generally* MPEP 2113. Here, it is not clear whether the malonyl group is required in the resulting product even though the step is there because Applicants do not recite a “malonyl-pegylated” (or similar suitable language) fullerene, etc. Thus, it is not clear what the method ultimately produces and whether there are additional unclaimed steps needed to achieve that end. Claims 18-19 import the issues of Claim 17.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

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1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

I. Claims 1 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,471,942 to Miller, et al.

With respect to Claim 1, this claim requires “[a] pegylated and hydroxylated trimetallic nitride endohedral metallofullerene comprising a plurality of hydroxyl groups and one or more polyethylene glycol moieties covalently bonded to a fullerene encapsulating a trimetallic nitride.” Miller teaches “trimetallic nitride template metallofullerenes” (Miller 2: 48-49). The fullerene can be functionalized with PEG and hydroxyl groups. (Miller 3: 20-25). Miller states that absorption is accomplished “by attaching *at least one functional group* to the fullerene cage.” (Miller 3: 17-18). Thus, to the extent Miller doesn’t disclose the precise combination recited in the claim, one of skill in the art would recognize the combination as an obvious expedient in view of the listing provided by Miller.

Claim 20 is a product-by-process claim. While process limitations are given weight, the claim requires only a pegylated trimetallic nitride endohedral metallofullerene that is hydroxylated. These features have been addressed in connection with Claim 1. *See also* Claim Rejections - 35 U.S.C. 112 *supra*.

II. Claims 5-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 6,471,942 to Miller, et al. as applied to claim 1 above, and further in view of Tabata, et al., *Biological functions of fullerene*, Pure Appl. Chem. 1999; 71(11): 2047-2053 (hereinafter “Tabata at ___”).

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The discussion of Claim 1 and Miller set forth in the obviousness rejection (“I”) *surpa* is expressly incorporated herein by reference. With respect to Claims 5-6, note that Miller explicitly states that polyethylene glycol functional groups are useful for enhancing adsorption of the fullerenes. (Miller 3: 14-31). To the extent Miller doesn’t go into such details as molecular weight and the particular PEG moieties, these are recognized in the art. *See* (Tabata at 2049) (“Preparation of C₆₀-PEG Conjugate”). A molecular weight of 5460 is being interpreted as “about” 5000. *Id.* Methoxy-PEG is also disclosed. *Id.* Note also the similar uses to those described in Miller, namely biological, *i.e.* injecting something into the body. *See e.g.* (Tabata “Abstract”). Note also the apparent routine use of PEG. (Tabata at 2048) (“Poly(ethylene glycol) (PEG) was selected as the water-soluble polymer for C₆₀ conjugation because it has been widely used for chemical modification of drugs due to simple conjugation chemistry.”) (citations omitted).

Allowable Subject Matter

I. Claims 2-4 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

The following is a statement of reasons for the indication of allowable subject matter: Claims 2-4 all require a malonyl moiety in some combination with a polyethylene glycol moiety. As discussed above, polyethylene glycol and its use in fullerene chemistry as facilitating dispersal or solubility is well known. Miller and Tabata are exemplary. Similarly, introduction of malonyl groups is well described in the literature. Malonyl groups are introduced through what is referred to in the art as a “Bingle-Hirsch” reaction. *See* US 6,355,225 to Alford at 8: 44 *et seq.*

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This is apparently a commonly employed synthetic technique. *See e.g.* US 2003/0065206 to Bolskar, et al. While this chemistry is known, the search of the prior art did not reveal introducing polyethylene glycol in this manner, *i.e.* with malonate chemistry or a “Bingle-Hirsch” reaction. Thus, while there might be structural similarity between the claims and metallofullerenes of *e.g.* Miller, the absence of a teaching of how to make it was considered persuasive in a finding of non-obviousness. *See* MPEP 2144.09 IV (“[T]he presence—or absence—of a suitably operative, obvious process for making a composition of matter may have an ultimate bearing on whether that composition is obvious—or nonobvious—under 35 U.S.C. 103.” *In re Maloney*, 411 F.2d 1321, 1323, 162 USPQ 98, 100 (CCPA 1969).”).

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Fatouros, et al., *In Vitro and in Vivo Imaging Studies of a New Endohedral Metallofullerene Nanoparticle*, Radiology 2006; 240(3): 756-764 is clearly relevant, but is not prior art in light of Applicants PCT filing date of 3/25/2005.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DANIEL C. MCCracken whose telephone number is (571)272-6537. The examiner can normally be reached on Monday through Friday, 9 AM - 6 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Stanley S. Silverman can be reached on (571) 272-1358. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Daniel C. McCracken/
Daniel C. McCracken
Examiner, Art Unit 1793
DCM